The following is the abstract of the article discussed in the subsequent letter:

El Midaoui, Adil, Jean Louis Chiasson, Gilles Tancreède, and André Nadeau. Physical training reverses defect in 3-ketoacid CoA-transferase activity in skeletal muscle of diabetic rats. Am J Physiol Endocrinol Metab 288: E748–E752, 2005; doi:10.1152/ajpendo.00515.2005.—To investigate one potential mechanism whereby physical training improves the plasma concentration of ketone bodies in experimental diabetes mellitus, we measured the activity of 3-ketoacid CoA-transferase, the key enzyme in the peripheral utilization of ketone bodies. Diabetes was induced with streptozotocin (50 mg/kg) and training carried out on a treadmill with a progressive 10-wk program. Diabetes resulted in an increase (P < 0.001) in plasma concentration of β-hydroxybutyric acid in sedentary rats, which was partly reversed by training (P < 0.001). Diabetes was also associated with a decreased activity of 3-ketoacid-CoA-transf erase in gastrocnemius muscle. When expressed per total gastrocnemius, training increased the activity of 3-ketoacid CoA-transferase by 66% in nondiabetic rats (P < 0.001) and by 150% in diabetic rats (P < 0.001), the decrease present in diabetic rats being fully reversed by training. Simple linear regression between the log of 3-ketoacid CoA-transferase activity and the log of plasma β-hydroxybutyric acid levels showed a statistically significant (r = 0.563, P < 0.001) negative correlation. The beneficial effects of training on plasma ketone bodies in diabetic rats are probably explained, at least in part, by an increase in ketone body utilization, mediated by an increase in skeletal muscle 3-ketoacid CoA-transferase activity.

Interpreting the overall metabolic consequences of exercise in diabetes

To the Editor: I read with great interest the important and carefully designed study by El Midaoui et al. (1). This study is the first to have prudently evaluated the effects of regular exercise on 3-ketoacid CoA-transferase activity in gastrocnemius muscle in the streptozotocin model of diabetes. They observed that the activity of 3-ketoacid CoA-transferase, expressed as either micromoles of acetooxalyl-CoA in minutes per gram or minutes per muscle, was reduced by the sedentary diabetic state, explaining the hyperketonemia seen in this condition. However, the authors reported an increase, following 10 weeks of regular aerobic exercise, in the activity of 3-ketoacid CoA-transferase in the vicinity of nearly 150%. This chronic adaptive change undoubtedly provides a mechanism accounting for the prevention of hyperketonemia in this model of diabetes (2).

There is no question that the authors have collected their data with usual attention to detail. My concerns, however, relate solely to the interpretation of the overall metabolic consequences of the increased ketone body utilization.

Thus, in the last paragraph on p. E751, the authors state that “the lower levels of free fatty acids in trained diabetic rats observed in the present study could thus also partly explain their low levels of β-hydroxybutyric acid.” Although a 40% reduction in the levels of free fatty acids represents a substantial change, this would also promote a greater reliance of tissues on glucose metabolism, which is typically reduced in diabetes. Using comparable exercise protocols and severities of the diabetic state, Hall et al. (3), Paulson et al. (4), Nakia et al. (5), and recently our group (6) have unequivocally demonstrated that the inhibitory effect of elevated fatty acid levels on glucose metabolism, characteristic of insulinopenia, can be overcome with aerobic exercise. Regular exercise is associated with both increased glucose transporter content and pyruvate dehydrogenase activity and, consequently, improved glucose oxidation. These changes not only restore the abnormal energy pattern, but also improve efficiency of fuel utilization in diabetes. The interpretation of their data, although eloquently presented and thorough, fails to mention this fundamental relationship that is critical in diabetes.

REFERENCES


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Letters To the Editor